



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/571,291

11/28/2006

Pascale Gaillard

GAILLARD2

6383

1444 7590 06/29/2011

Browdy and Neimark, PLLC
1625 K Street, N.W.
Suite 1100
Washington, DC 20006

EXAMINER

BALASUBRAMANIAN, VENKATARAMAN

ART UNIT

PAPER NUMBER

1624

MAIL DATE

DELIVERY MODE

06/29/2011

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

ADVISORY ACTION

The applicants' response filed 06/15/2011 under 37 CFR 1.116 in reply to the final rejection has been considered but is not deemed to place the application in condition for allowance. Claims 1-8 and 11-13 are now pending. Applicants' traversal to overcome the 103 rejection made in the previous office action is not persuasive and the rejection is maintained.

Claims 1-8 and 11-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Halazy et al., WO 01/47920 in view of Bennett et al., Current Opinion in Pharmacology 2003, 3:420–425(or Kaneto-I, Kaneto-II, Kaneto-III or Hotamisligil) and Gatlin et al., US 6,559,188 for reasons of record.

This rejection is same as made in the previous office action but limited to currently pending claims.

Applicants' traversal to overcome this rejection is not persuasive.

Applicants have asserted that "While Bennett, Kaneto-I, Kaneto-II, Kaneto-II and Hotamisligil teach that the JNK pathway may be involved in diabetes and insulin resistance, using various genetic evidence or biomolecular tools, these references do not teach that a JNK inhibitor would however treat such diseases".

This is assertion is not persuasive, clearly lacks factual support and contradicts what is known in the art. It is well known in the art that inhibitor of activity of a target implicated in disease would be useful in treating the disease.

This is clearly evident even from the title of Bennett's review article, which reads JNK: a new therapeutic target for diabetes.

The all references cited also lend support for this fact.

For example, Kaneto-I, teaches the role of JNK and its inhibitors in diabetes in pages 431-432 citing references 62-77 and Kaneto-II teaches the role of JNK and its inhibitors in diabetes in pages 581-585 citing references 8-89 and Kaneto-III teaches the role of JNK and its inhibitors in diabetes in pages 167-174 citing references 65-84. Hotamisligil also teaches the role of JNK and its inhibitors in diabetes in pages 167-174 citing references 65-84. All these references are prior art. The cited references are review articles which relate role of Janus kinase in diabetes and they provided number of references which are earlier than instant effective priority date.

In short, the compounds taught by Halazy are same as that of instant claims. Instant specification on page 2 clearly acknowledges this. The compounds of Halazy are JNK inhibitors. Thus, administering the genus of compounds of Halazy (that is instant genus of compounds) would inhibit JNK. Whatever negative attributes applicants offer for method of use of compounds of Halazy would be equally applicable to instant compounds.

Bennett et al., clearly teaches JNK inhibitors to be useful in treating insulin resistance, diabetes and obesity as seen pages 420-422. Instant claims recite the same. Applicants argued, pointing page that while instant compounds decreases insulin and glucose, Bennett teaches lowering of plasma glucose but not plasma insulin. This is not correct. Contrary to applicants' urging, the Figure 2 shown in page 422 of Bennett clearly shows lowering of plasma glucose and insulin. And it is also improper comparison as applicants have measured plasma glucose level and plasma insulin level

after 4 hr as pointed by applicants(see page 29, lines 18-21).

Contrary to applicants' urging, Bennett in this column clearly teaches usefulness of JNK inhibitors in treating insulin resistance, diabetes and obesity as reproduced below:

"We have studied the performance of a small molecule JNK inhibitor (Celgene Corporation; CC105) in the leptin-receptor-deficient model of diabetes and obesity, the db/db mouse. This strain exhibits an early-phase hyper- insulinemia followed by progressive pancreatic failure and hypoinsulinemia from about six weeks of age. This leads to increased blood glucose and obesity. After 17 days of oral dosing with the JNK inhibitor, we observed significantly lower blood glucose and higher insulin levels (Figure 2). After oral glucose loading, we observed increased plasma insulin and improved glucose control in animals treated with the JNK inhibitor (Figure 2). Ex vivo analysis of pancreatic islet cells showed marked improvements in acinar recovery and morphology, as well as insulin release following high glucose stimulation (Figure 3). This preliminary pharmacological data shows striking parallels to the observations made using Jnk1-l- ob/ob mice. Further studies in appropriate models should define the potential of JNK inhibitors in treating insulin resistance and obesity".

Clearly, based on the significant lowering of blood sugar, one would expect JNK inhibitors to be useful for treating Type-II diabetes and obesity. The entire document and especially the concluding paragraph clearly lend support for JNK inhibitors to treat diabetes, insulin resistance and obesity. It is held that, although there is no reason to doubt the compounds of Halazy were not useful for treating insulin resistance, even if

they were not useful for treating insulin resistance, the compounds of Halazy would be useful for treating diabetes and obesity.

Similarly, the all the secondary references Kaneto-I, Kaneto-II, Kaneto-III and Hotamisligil teach usefulness of JNK inhibitors for treating Type-II diabetes. See entire document.

Applicants have also argued citing Mihai that salicylate may increase insulin resistance (see first column on page 1723) and also negatively influence insulin sensitivity (third column of page 1723) through other mechanisms. This is not relevant. What is relevant is the teaching that JNK inhibitors are useful for treating diabetes. Furthermore, the fact that SP600125 has other mode of action besides mode of action as JNK inhibitors is not relevant as the issue here is will one trained in the art consider a JNK inhibitors useful for treating diabetes.

Applicants' argument that "It is clear that compounds not structurally related, like SP600125 and the compounds of the present invention, have different selectivity profiles and thus different pharmaceutical properties. Thus, it cannot be deduced from the specific example of SP600125 that any JNK inhibitor, including the structurally unrelated compounds presently claimed, would have the same effect". This is also not persuasive argument. Compounds taught by Halazy are same as instant compounds and therefore would share the same profiles as instant compounds.

Applicants' also asserts that "It is further pointed out that it is not enough to have identified that the JNK pathway may be involved in diabetes in order to conclude that any JNK inhibitor would effectively treat diabetes, especially since there is much in the

way of complex and unforeseeable mechanisms of regulation that may occur". Again compounds taught by Halazy are same as instant compounds and therefore would share the same profiles as instant compounds.

In summary, Halazy teaches a genus of compounds useful as JNK inhibitors and all references cited above teach JNK inhibitors are useful for treating diabetes. Hence, one trained in the art would be motivated to make the genus of compounds taught by Halazy and expect them to be useful for treating diabetes in view of the teachings of the secondary references.

For reasons stated above this rejection is proper and is maintained.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For

Art Unit: 1624

more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

/Venkataraman Balasubramanian/

Primary Examiner, Art Unit 1624